treated with chlorambucil alone. This does not exclude the possibility of deleterious effects on other tissues, in particular the gonads.[5]

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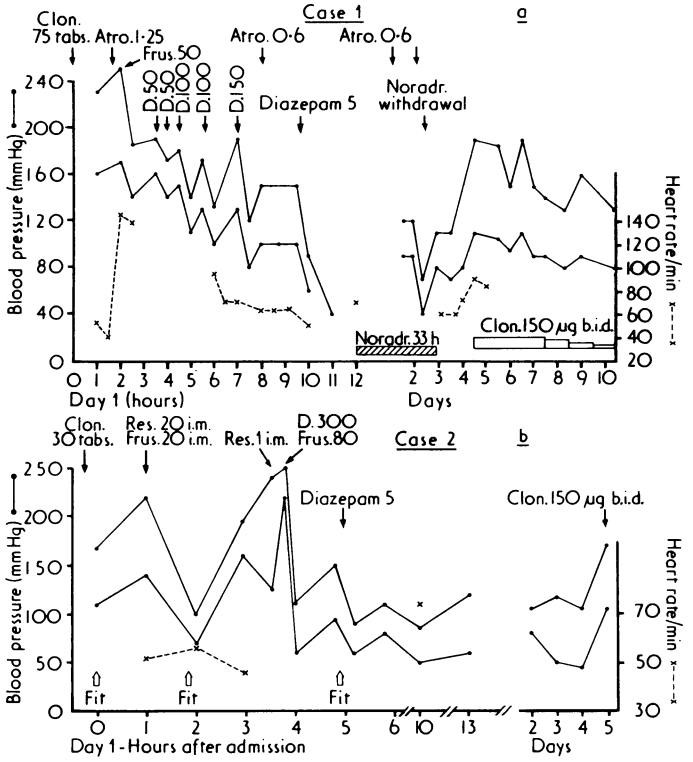
Clonidine overdose

Clonidine acts at central[1] and peripheral[2] sites and affects plasma renin and catecholamines. Doses up to 5 mg/day have been used in resistant hypertensives. In some patients the sudden cessation of clonidine causes a severe rebound rise in blood pressure within 24 hours.[3] During such an episode there is evidence of excessive sympathetic discharge which could be related to the alphamimetic action of the drug.[2 4] We describe patients with clonidine overdose in whom it was not known whether the alpha-mimetic or hypotensive effects of the drug would predominate in the early stages. Late rebound hypertension was not observed in either case.



Time course of blood pressure and heart rate in (*a*) case 1 and (*b*) case 2. Clon. = Clonidine 150 µg tablets. Atro. = Atropine mg intravenously. Frus. = Frusemide mg intravenously. D. = Diazoxide mg intravenously. Noradr. = Noradrenaline infusion, 2 ml/min of 1:2 500 000. Res. = Reserpine.

Case Reports

Case 1.—A previously normotensive 17-year-old girl took 75 clonidine tablets (150 µg), after which she became increasingly drowsy. The blood pressure on admission was 230/160 mm Hg and the heart rate was 52/min. Subsequent blood pressures and heart rates are shown in the Fig. In the eight hours after admission atropine 1·25 mg intravenously was given for bradycardia (40/min) and intravenous diazoxide (total 450 mg) and intravenous frusemide 50 mg were given for hypertension. A hypotensive phase followed an injection of 5 mg intravenous diazepam and a noradrenaline infusion was required for 33 hours to maintain blood pressure. On the fifth day in hospital the blood pressure rose to 190/110 mm Hg. Clonidine 150 µg twice a day was began and progressively reduced with maintenance of normal blood pressure. Hyperglycaemia (38·9 mmol/l (700 mg/100 ml); Somogyi-Nelson method), noted after a total of 450 mg diazoxide, responded to soluble insulin. Hypothermia, initially 32·5°C rectally, persisted for 48 hours. A 24-hour urine sample yielded 5·3 mg of clonidine, which represented nearly half the ingested dose.

Case 2.—A second 17-year-old girl with documented renal failure had been started on clonidine 75 µg twice a day two years earlier because of a mild blood pressure increase of 150/100 mm Hg. Recent blood pressure control was good on the same antihypertensive regimen. She took 30 clonidine tablets (150 µg each) and 10 minutes later fell asleep. Eight hours after taking the overdose she had a generalized convulsion, which recurred twice. Two blood pressure peaks of 220/140 and 240/125 mm Hg unrelated to the fits were treated with reserpine 1 mg intramuscularly, but on the second occasion the blood pressure continued to rise, reaching 250/215 mm Hg. At that stage diazoxide 300 mg and frusemide 80 mg were given intravenously and this treatment effectively reduced the blood pressure to normal. The blood pressure stayed in the low normal range for the next three days, but rose to 170/105 mm on the fifth day, when clonidine 150 µg twice a day was begun (see Fig.). At follow-up examination six weeks later the blood pressure was 140/100 mm Hg.

Comment

These two cases illustrate that clonidine overdose (of 30 tablets or more of 150 µg each) results, within a few hours, in a severe increase in blood pressure with diastolic levels over 150 mm Hg. This response is probably related to the dominance of the well-known alpha-mimetic action of clonidine[4] over its central sympathetic inhibitory hypotensive action[1] in the presence of high serum levels of the drug. This pressor reaction responds satisfactorily to adequate doses of diazoxide. One patient had chronic renal failure and hypertension before taking the clonidine overdose. It is possible that a given pressor stimulus has a more pronounced effect in patients with pre-existing hypertension, in whom there may already be an unfavourable alteration in vessel wall: lumen ratio.[5]

Both patients survived despite large doses of clonidine which had profound blood pressure and heart rate effects. The early hypertensive phase responded adequately to diazoxide, and in one patient late hypotension required treatment with a pressor agent. This hypotensive phase could have resulted from an interplay of factors, such as the administration of intravenous diazepam. Small doses of oral clonidine were used to tide the patients over the withdrawal phase, until their baseline blood pressures were re-established. Both patients had severe and recurring bradycardia with rates as low as 40/min.

Forced frusemide diuresis seems to be an effective means of removing clonidine. In the first patient almost half the ingested drug was excreted by this method within 24 hours. Forced frusemide diuresis is effective in the presence of normal renal function and will not obviate the need for specific treatment of bradycardia, hypothermia, hyperglycaemia, hypotension, and possible rebound hypertension.

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